EXHIBIT C

SUMMARY OF THE INVENTION

The invention encompasses methods of treatment of various conditions susceptible of treatment with an interferon, involving administering to a mammal, preferable a human, a therapeutically effective amount of consensus human leukocyte interferon (IFN-con). The invention is based on the discovery that IFN-con does not cause the same degree of side effects in patients as do alpha interferons. The conditions that may be treated in accordance with the present invention are generally those that are susceptible to treatment by alpha interferons. In other words, IFN-con is useful to treat substantially the same conditions that may be treated with alpha interferons, such as Intron® A. Exemplary conditions include, but are not limited to, cell proliferation disorders and viral infections. IFN-con is effective in treating cell proliferation disorders frequently associated with cancer. Such disorders include, but are not limited to, hairy cell leukemia and Kaposi's Sarcoma. IFN-con may be used alone or in combination with other therapeutics for the treatment of cancer and other proliferative disorders. In a preferred embodiment, IFN-con is used in conjunction with a therapeutically effective amount of one or more factors that stimulate myeloid cell proliferation or differentiation, such as granulocyte colony stimulating factor (G-CSF), granulocyte/ macrophage colony stimulating factor (GM-CSF), interleukin-1 (IL-1), interleukin-3 (IL-3), interlenkin-6 (IL-6), erythropoietin, and stem cell factor (SCF). G-CSF is a preferred factor for use with IFN-con.

Viral conditions treatable by IFN-con include, but are not limited to, hepatitis A, hepatitis C, other non-A, non-B hepatitis, hepatitis B, herpes virus (EB, CML, herpes simplex), papilloma, poxvirus, picorna virus, adeno virus, rhino virus, HTLV I, HTLV II, and human rotavirus.

Although it has previously been appreciated that the above conditions can be treated with alpha interferon, side effects accompanying such treatment have severely limited the overall usefulness of such treatment. In some cases, such as Epstein-Barr infection, side effects accompanying alpha interferon treatment have virtually ruled out treatment using alpha interferon. Thus, for purposes of the present invention, conditions that can be treated with IFN-con include those conditions in which alpha interferon treatment shows some efficacy, but which may not be treatable with known interferons because the negative side effects outweigh the benefits of the treatment. It has now been discovered and disclosed herein that treatment with a non-naturally occurring interferon, selected from consensus human leukocyte interferons (IFN-con) results in substantially reduced or eliminated side effects as compared to treatment with alpha interferon. The reduction or elimination of side effects is expected to be demonstrated regardless of the condition being treated. The reduction or elimination of side effects discovered for IFN-con could not have been predicted based on the results reported in the prior art. The actual clinical results presented herein clearly demonstrate not only that IFN-con causes reduced or non-existent side effects at the same dose level as alpha interferon, but that 3 to 5 times more IFN-con may be administered without causing dose-limiting side effects.

Additionally, it is shown below that IFN-con has similar or higher activity than INTRON® A in the above described indications. In particular, IFN-con shows higher antiproliferative activity than INTRON® A. Therefore, treatment of a cell proliferation disorder using IFN-con shows enhanced efficacy and safety compared to other currently practiced interferon treatments. The administration of a therapeutically effective amount of IFN-con results in more rapid or more extensive treatment of a cellular proliferative disorder compared to currently practiced methods, wherein no corresponding increase in the frequency or severity of associated undesirable side effects occurs. In addition, a therapeutically effective amount of IFN-con may be less than the amount of an interferon used in currently practiced regimens. As a result, in some cases, a decreased dose of IFN-con gives the same therapeutic benefit as higher doses of other interferons but with a decrease or elimination of undesirable side effects associated with currently practiced interferon therapy.

IFN-con is a nonnaturally-occurring polypeptide having antiproliferative activity. Preferably, IFN-con is a polypeptide having the amino acid sequence of IFN-con$_1$, IFN-con$_2$, or IFN-con$_3$. Most preferably, IFN-con has the amino acid sequence of IFN-con$_1$.

The invention also relates to pharmaceutical compositions comprising a therapeutically effective amount of IFN-con along with suitable diluents, adjuvants, carriers, preservatives and/or solubilizers.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows the antiproliferative activity of IFN-con$_1$ and INTRON®A, a comparative material, on Eskol, a hairy cell leukemic cell line, when interferons were added to an Eskol cell suspension at 0.1 ngs/ml.

FIG. 2 shows the antiproliferative activity of IFN-con$_1$ and INTRON®A, a comparative material, on Eskol, a hairy cell leukemic cell line, when interferons were added to an Eskol cell suspension at 0.5 ngs/ml.

FIG. 3 shows the antiproliferative activity of IFN-con$_1$ and INTRON® A, a comparative material, on Eskol, a hairy cell leukemic cell line, when interferons were added to an Eskol cell suspension at 1.0 ngs/ml.

FIG. 4 shows the antiproliferative activity of IFN-con$_1$ and INTRON® A, a comparative material, on Eskol, a hairy cell leukemic cell line, when interferons were added to an Eskol cell suspension at 5.0 ngs/ml.

FIG. 5 shows the antiproliferative activity of IFN-con$_1$ and INTRON® A, a comparative material, on Eskol, a hairy cell leukemic cell when interferons were added to an Eskol cell suspension at 10 ngs/ml.

FIG. 6 shows the antiproliferative activity of IFN-con$_1$ and INTRON®A, a comparative material, on Eskol, a hairy cell leukemic cell line, when interretorts were added to an Eskol cell suspension at 50 ngs/ml.

FIG. 7 shows the antiproliferative activity of IFN-con$_1$ and INTRON® A, a comparative material, on Eskol, a hairy cell leukemic cell line, when interferons were added to an Eskol cell suspension at 100 ngs/ml.

FIG. 8 shows the first and current median MTDs achieved by Kaposi's Sarcoma patients treated with INTRON-A, IFN-Con$_1$, or IFN-Con$_1$ and r-metGCSF.

DETAILED DESCRIPTION OF THE INVENTION

As employed herein, consensus human leukocyte interferon (IFN-con) means a nonnaturally-occurring polypeptide, which predominantly includes those amino acid residues that are common to all naturally-